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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/661,939
Filing Date: September 12, 2003
Appellant(s): SKRALY, FRANK A.

Patrea L. Pabst
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/27/2007 appealing from the Office action mailed 5/1/2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

No amendment after final has been filed.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Whisstock et al. Quaterly Reviews of Biophysics, 2003, "Prediction of protein function from protein sequence and structure", 36(3): 307-340.

Branden et al. Introduction to protein structure, Gerald Publishing Inc., New York, page 247, 1991.

Witkowski et al. Conversion of a beta-ketoacyl synthase to a malonyl decarboxylase by replacement of the active-site cysteine with glutamine, Biochemistry. 1999 Sep 7; 38(36):11643-50.

Seffernick et al. Melamine deaminase and atrazine chlorohydrolase: 98 percent identical but functionally different, J Bacteriol. 2001 Apr; 183(8):2405-10.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 16-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 16 and 21-23 are directed to a recombinant organism comprising and expressing a heterologous gene encoding any CoA-dependent aldehyde dehydrogenase from any source.

Claim 17 recites that the said organism further comprises a gene encoding any PHA synthase and claim 18 recites that said organism further comprises one or more genes encoding enzymes selected from the group consisting of acyl-CoA transferase, acyl-CoA synthetase, β-ketothiolase and acetoacetyl-CoA reductase. Claims 19 and 20 recite that the one or more genes claimed in claim 18 are either endogenous or heterologous to said organism As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the structure of only a single representative species of gene encoding CoA-dependent aldehyde dehydrogenase, three representative species of PHA synthase, single representative species of acyl-CoA transferase, single representative species of acyl-CoA synthetase, single representative species of β-ketothiolase and single representative species of acetoacetyl-CoA reductase. Moreover, the specification fails to describe any other representative species by sufficient identifying characteristics or properties other than the functionality of encoding CoA-dependent an aldehyde dehydrogenase, PHA synthase, acyl-CoA transferase, acyl-CoA synthetase, β-ketothiolase and acetoacetyl-CoA reductase. Given this lack

of description of representative species encompassed by the genus of DNAs used in the said recombinant organism, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 16-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant organism comprising a plasmid expressing a heterologous CoA-dependent aldehyde dehydrogenase gene eutE from E. coli and endogenous PHA synthase gene or a heterologous PHA synthase gene from Aeromonas caviae, does not reasonably provide enablement for a recombinant organism comprising a plasmid having any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase gene or any acyl-CoA transferase gene or any acyl-CoA synthetase or any β-ketothiolase or any poly(4-hydroxybutyrate) synthase and any acetoacetyl-CoA reductase from any source having any structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 16-23 are so broad as to encompass a recombinant organism comprising a plasmid having any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase gene or any acyl-CoA transferase gene or any acyl-CoA synthetase or any β-ketothiolase or any poly(4-hydroxybutyrate) synthase and any acetoacetyl-CoA reductase from any source having any structure. Claim 17 recites that the said organism further comprising any gene encoding any PHA synthase and claim 18 recites that the said organism further comprising genes encoding

enzymes selected from the group consisting of any acyl-CoA transferase, any acyl-CoA synthetase, any β-ketothiolase and any acetoacetyl-CoA reductase and claim 19 recites that one or more genes are endogenous. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of aldehyde dehydrogenase gene (CoA-dependent), PHA synthase gene or poly(4-hydroxybutyrate) synthase or acyl-CoA transferase gene or acyl-CoA synthetase or β-ketothiolase and acetoacetyl-CoA reductase gene broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequences of only one aldehyde dehydrogenase gene (CoA-dependent), one acyl-CoA transferase gene or one acyl-CoA synthetase or one β-ketothiolase and one acetoacetyl-CoA reductase gene and three PHA synthase gene.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and

additional modification, e.g. multiple point mutations or substitutions.

The specification does not support the broad scope of the claims which encompass any recombinant organism or any recombinant bacteria or any recombinant plant comprising a plasmid having any aldehyde dehydrogenase gene (CoA-dependent), any PHA synthase gene or any acyl-CoA transferase gene or any acyl-CoA synthetase gene or any β-ketothiolase gene and any acetoacetyl-CoA reductase gene because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting polypeptide activity; (B) the general tolerance of polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any aldehyde dehydrogenase or any acyl-CoA transferase or any acyl-CoA synthetase or any β-ketothiolase and any acetoacetyl-CoA reductase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any recombinant organism or any recombinant bacteria or any recombinant plant comprising a plasmid having any CoA-dependent aldehyde dehydrogenase gene or any acyl-CoA transferase gene or any acyl-CoA synthetase gene or any β-ketothiolase gene and any acetoacetyl-CoA reductase gene. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any recombinant organism or any recombinant bacteria or any recombinant plant comprising a plasmid having any said genes having the desired biological

characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

(10) Response to Argument

A.) Rejection of claims 16-23 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 16 and 17

On page 8 of the brief, appellant traverses the rejection on the grounds that Claims 16 and 17 define a recombinant organism selected from the group consisting of bacteria, yeast, fungi and plants for producing polyhydroxyalkanoates, comprising a heterologous gene encoding a Co-A-dependent aldehyde dehydrogenase and a PHA synthase and further argue that it is clear from the disclosure in the specification, that one of ordinary skill in the art would conclude that Appellants were in possession of the claimed organisms because the enzymes defined by the claims are well-known, exist within well-defined classes of proteins, and the genes encoding them are known and described in the literature.

This is not found persuasive because claims 16-23 are directed to a recombinant organism comprising and expressing a heterologous gene encoding any CoA-dependent aldehyde dehydrogenase and any PHA synthase from any source having any structure for producing polyhydroxyalkanoates (PHAs). While appellants argue that claims are drawn to genes or

enzymes, which are well known in the art and the specification provide ample evidence of the structural feature of the recited genes encoding enzymes such as CoA-dependent aldehyde dehydrogenase and PHA synthase, claims rejected are drawn to microorganisms comprising said enzymes, whose structures are indeed not disclosed. Claims still read on a microorganism comprising any CoA-dependent aldehyde dehydrogenase and any PHA synthase i.e. claims are having only functional feature and lacks structural feature. In order to satisfy Written Description requirement, Applicants are required to disclose adequate description of the specific structural feature of the genus (genes) used to make the organism; such that one of the ordinary skill in the art can easily practice the claimed invention. If the genus (genes) of polynucleotides expressing the enzymes is not described adequately, then organisms comprising the same are also not described. In addition, the microorganisms used in the method comprising the genus of any CoA-dependent aldehyde dehydrogenase and any PHA synthase are a very large genus having different structures. In the instant case claim 16 reads on a microorganism comprising any CoA-dependent aldehyde dehydrogenase and any PHA synthase i.e. there is no structural feature, which is representative of all the members of the heterologous CoA-dependent aldehyde dehydrogenase and PHA synthase recited in the claim. Many variants and mutant polypeptides with varied structure are encompassed by the recited genus. The specification teaches the structure of a single CoA-dependent aldehyde dehydrogenase isolated from E. coli and the structure of a single PHA synthase isolated from Aeromonas caviae, having the respective functional characteristics, which is insufficient to adequately describe the structure of required genus of heterologous CoA-dependent aldehyde dehydrogenase and PHA synthase having recited functional characteristics.

Appellant also argues that the words "PHA synthase," and "Co-A-dependent aldehyde dehydrogenase" classify proteins and readily convey distinguishing information concerning identity, *via* structure and function, such that one of ordinary skill in the art could easily visualize the identity of the members of each classification. Appellants further argue that it is well known to those of ordinary skill in the art that functional definitions do provide structural information commonly possessed by all members of each class, especially as applied to enzymes. This is not found persuasive because appellant has not provided any sequence alignment data by which one of ordinary skill in the art could predict the structural feature of the claimed genus of any CoA-dependent aldehyde dehydrogenase and any PHA synthase. It is well known in the art that the same protein function can be provided by many unrelated protein structures. Thus, the disclosure of several genes having the recited function in the specification and/or the art clearly does not put a skilled artisan in possession of all the diversity of protein structures, which will provide for that function. At best, it would provide a skilled artisan a genus of enzymes structurally similar to those disclosed in the specification and/or the art. For evidence of this see Whisstock et al. (2003), who disclose that for proteins, similar sequences determine similar structures but much less reliable is the widely held assumption that similar sequences should have similar functions, that the assumption that similar sequences share similar function is less safe as the sequences diverge, but that even very similar sequence can have very different functions and most importantly here that similar functions are often carried out by proteins with dissimilar structures (see particularly pages 309-310 of Whisstock et al.). Besides, Appellants drawings do not show any sequence homology data that would support the notion that one of ordinary skill in the art would predict the structures of any CoA-dependent aldehyde dehydrogenase and any PHA

synthase. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient structure and variety of species to reflect the representative structure variation within the genus.** Satisfactory disclosure of a representative structure and number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, cannot be achieved by disclosing the structure of small portion of only one species within the genus. The genus of polypeptides of any CoA-dependent aldehyde dehydrogenase and any PHA synthase used in making the claimed recombinant organism are structurally diverse as it broadly encompasses many mutants and variants comprising respective enzyme activity having different structures. As such, the disclosure solely of functional features, is insufficient to be representative of the attributes and features of the entire genus.

Furthermore, Appellant argues that a claim is not unpatentable simply because the "embodiments of the specification do not contain examples explicitly covering the full scope of

the claim language. This is not found persuasive because appellants were never required to show that the specification contains examples explicitly covering the full scope of the claim language. The rejection states that the specification fails to disclose sufficient species to be representative of the full scope of the claims. Since the claims recite functional features only, the specification and/or art must clearly provide a correlation between structure and function such that a skilled artisan would be put in possession of the structure of other members of the genus. No such structure to function correlation has been provided. Although, the embodiments do not need to explicitly cover all the species of the claimed genus, the specification does need to disclose sufficient species to be representative of the diversity of structures encompassed by the full scope of the claims. The PHA synthase and CoA-dependent aldehyde dehydrogenase genes known in the art fail to provide sufficient species for the reasons discussed above..

Appellants also argue that the specification actually describes a representative number of the enzymes in each class and provides numerous sources of a CoA-dependent aldehyde dehydrogenase, including accession numbers and PHA synthase genes for the development of recombinant producers are known in the art. This is not found persuasive because claims still read on a microorganism comprising any CoA-dependent aldehyde dehydrogenase and any PHA synthase i.e. claims are having only functional feature and lack structural feature, which is required to satisfy written description requirement. It is well known in the art that the same protein function can be provided by many unrelated protein structures such that the genes of the prior art clearly do not put a skilled artisan in possession of all the diversity of protein structures, which will provide for the recited function. Many of the structures unrelated to those of the prior art will provide CoA-dependent aldehyde dehydrogenase and PHA synthase function. Each of

the prior art genes at best is representative of a genus of genes encoding structurally similar proteins which retain the recited functions. However, this is clearly not representative of the many other species of the genus whose structures are unrelated to these genes. Besides, Appellants drawings do not show any sequence homology data that would support the notion that one of ordinary skill in the art would predict the structures of any CoA-dependent aldehyde dehydrogenase or any PHA synthase to practice the claimed invention.

Furthermore, in *University of California v. Eli Lilly & Co., 43 USPQ2d 1938*, the court of appeals for the Federal Circuit has held that " A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise defination, such as by structure, formula, or chemical name,' of the claimed subject matter sufficient to distinmguish it from other materials". In the instant case, as previously indicated, the genus of genes encompassed by the claims is defined functionally, the genus of genes recited is not only very large but also ***structurally unrelated***. Neither the specification nor the art provide a correlation between structure and function sufficient to allow one of ordinary skill in the art to envision the structure of any CoA-dependent aldehyde dehydrogenase and any PHA synthase using the structures of known genes or those disclosed in the specification.

The specification teaches the structures of several representative species of CoA-dependent aldehyde dehydrogenase and several representative species of PHA synthase, having the respective functional characteristics, which is insufficient to adequately describe the structure of the required genus of heterologous any CoA-dependent aldehyde dehydrogenase and any PHA synthase having recited functional characteristics, which are not representative of the attributes and features of all the members of the genus used to make the claimed microorganism.

Claims 18-20

Regarding claims 18, 19 and 20, Appellants argue that the organism comprises recited genes encoding enzymes selected from the group consisting acyl-CoA transferase, acyl-CoA synthetase, beta-ketothiolase, and acetoacetyl-CoA reductase, which are either homologous or heterologous to the organism and furthermore, stated that all the genes are well known in the art. Appellants also argue that "there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure" (Capon v. Eshhar, 418 F.3d at 1358, 76 USPQ2d at 1084). Appellants furthermore, argue that "a patent need not teach, and preferably omits, what is well known in the art" (In Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524). This is not found persuasive because claims still read on using any acyl-CoA transferase, acyl-CoA synthetase, beta-ketothiolase, and acetoacetyl-CoA reductase having any structure and the claimed invention requires the structures of the genes recited, even though all the genes are well known in the art. In the absence of these genes, one of skill in the art would not practice the claimed invention. Furthermore, claims not only encompass these genes whose structures are known but they also encompass those genes whose structures are completely unknown. The issues in the instant application are not analogous to Capon v. Eshhar in view of the fact that the genus of products which have been found to lack adequate written description are not the same as those of Capon v. Eshhar. As stated in the Capon v. Eshhar decision. "[t]he descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of science. Since law is applied to each

invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science" (page 13, last paragraph, continuing on page 14). In *Capon v. Eshhar,* the genus of products at issue were chimeric genes encoding a single-chain Fv domain of an antibody and the transmembrane/cytoplasmic/extracellular domains of an endogenous protein. In the instant case, the genus of products at issue comprises genes encoding any acyl-CoA transferase, any acyl-CoA synthetase, any beta-ketothiolase, and any acetoacetyl-CoA reductase in addition of any CoA-dependent aldehyde dehydrogenase and any PHA synthase. *In University of California v. Eli Lilly & Co.,* 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". In the instant case, as previously indicated, while the genus of genes encompassed by the claims is defined functionally, the genus of genes recited is not only very large but also *structurally unrelated.* Neither the specification nor the art provide a correlation between structure and function sufficient to allow one of skill in the art to envision the structure of any gene encoding any acyl-CoA transferase, any acyl-CoA synthetase, any beta-ketothiolase, and any acetoacetyl-CoA reductase in addition of any CoA-dependent aldehyde dehydrogenase and any PHA synthase. using the structures of known genes or those disclosed in the specification.

Claim 21

Regarding claim 21, the Appellants argue that the limitation of the claim to E. coli eutE as the CoA-dependent aldehyde dehydrogenase limits the claim to that which the Examiner has

indicated is discussed. However, the rejection has been maintained for this claim because of the lack of structural feature of the heterologous PHA synthase gene recited. Although, claim 21 partially fullfils the written description requirement in the context of the CoA-dependent aldehyde dehydrogenase, it fails to sufficiently describe the genus of PHA synthase genes for all the reasons discussed above for claims 16 and 17..

Claims 22 and 23

Regarding claims 22-23, the appellants argue that claims specify recombinant organisms are bacteria or plant, which are suitable for production of PHAs that is well known in the art and described in the specification. However, the rejection has been maintained because claims are not further limiting the genus of genes encoding any CoA-dependent aldehyde dehydrogenase and any PHA synthase used to make the organism recited in claim 16. Furthermore, MPEP (1205) states that "merely pointing out what a claim recites will not be considered an argument for separate patentibility of the claim". Thus, all arguments above for claims 16 and 17 apply equally to claims 22 and 23.

B.) Rejection of claims 16-23 under 35 U.S.C. 112, first paragraph, for lack of enablement of the full scope of the claimed invention.

Claims 16 and 17

On page 17 of the brief, appellants traverse the rejection on the grounds that Appellants are addressing the problem of how to provide recombinant organisms that can produce high levels of medium chain length polyhydroxyalkanoates, while avoiding increasing the level of 3-hydroxyacid in the feed, avoiding the use of 3-propionic acid in the feed, and

avoiding the generation of free propionic acid in the cytosol, which in turn reduces the rate of production. This is not found persuasive because claims do not recite anything about avoiding of 3-hydroxyacid or 3-propionic acid rather claims are drawn to a recombinant organism comprising heterologous genes encoding any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase from any source having any structure for producing PHA.

Appellants argue that the specification discloses numerous sources for the enzymes recited in the claims. This is not found persuasive because claims still read on using any CoA-dependent aldehyde dehydrogenase or any PHA synthase from any source having any structure. One of ordinary skilled in the art would not know how to make the claimed invention without knowing the specific structural feature of the claimed genus of genes encoding any CoA-dependent aldehyde dehydrogenase or any PHA synthase from any source having any structure used to make the recombinant organism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of aldehyde dehydrogenase gene (CoA-dependent), and PHA synthase gene including many mutants and variants broadly encompassed by the claims. The claims encompass not only known DNAs but also unknown DNAs having structures unrelated to any of the genes disclosed in the specification or the art. It is reiterated herein that neither the specification nor the art have provided a structure/function correlation sufficient to allow one of skill in the art to envision the structure (or a significant portion thereof) of any DNA encoding the recited enzymes or the structure of any of the recited enzymes. To enable full scope of the claimed invention, the specification should provide one of skilled in the art with sufficient information to allow the

determination of those structures required or some teaching as to how to obtain those structures without undue experimentation.

Appellants argue that the examiner has failed to provide any evidence or reasoning as to why those skilled in the art would not extrapolate from the actual examples in the application to other aldehyde dehydrogenase, acyl-CoA transferase, acyl-CoA synthetase, 13-ketothiolase, acetoacetyl-CoA reductase and PHA synthase genes from other sources that are known in the art as evidenced by disclosure in the specification and literature cited and a skilled artisan, from the information in the art, would know which of the disclosed genes to use. This is not found persuasive because claimed genus of genes used to make the recombinant organism is highly variable genus which encompasses many genes having varied structures. One of the skilled in the art cannot extrapolate and make the claimed invention commensurate to the scope of the claim without undue experimentation. While, a skilled artisan may extrapolate a portion of the invention from the teaching of the disclosure (i.e., a skilled artisan could use the known genes to make minor variants of these genes and/or to isolate other highly structurally related genes from other organisms) a skilled cannot extrapolate from the disclosure of the specification and art to full scope of the claims as the full scope of the claims encompass vast numbers of genes with structures unrelated and not highly homologous to those known in the art which could not be made without undue experimentation.

Appellants also argue that it is unclear how using genes that are known, with known methods of heterologous expression to make the claimed organisms, cannot be enabled. This is not found persuasive because enablement for a claimed invention requires how to make the claimed invention commensurate to full scope of the claim. While the specification may enable use of

known genes, the claims encompass much more than this. Full scope of the instant claims encompasses not just known genes but also unknown genes which are unrelated to the known genes in structure. One of ordinary skill in the art would not know how to make the claimed organism without knowing the structural feature of the claimed genus of genes encoding any CoA-dependent aldehyde dehydrogenase or any PHA synthase from any source having any structure, which would require undue experimentation.

Furthermore, the Appellants argue that they are not claiming novel genes. The genes are known. A point of novelty here is that Appellants have provided organisms that can produce high levels of medium chain length polyhydroxyalkanoates while avoiding increasing the level of 3-hydroxyacid, by providing the organisms with the ability to also express in combination with the PHA biosynthesis genes, a CoA-dependent aldehyde dehydrogenase, to scavenge 3-hydoxyacids. This is not found persuasive because while it is agreed that the claims are not drawn to DNAs, however, recited DNAs are essential to practice the claimed invention. In absence of these DNAs, the claimed organism could not produce the required enzymes and the production of PHA could not take place. As stated previously, the specification does not reasonably provide enablement for a recombinant organism comprising a plasmid having any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase gene from any source having any structure. Thus, the claims encompass not only known DNAs but also unknown DNAs. It is reiterated herein that neither the specification nor the art have provided a structure/function correlation sufficient to allow one of skill in the art to envision the structure (or a significant portion thereof) of any DNA encoding the recited enzymes or the structure of any of the recited enzymes. To enable full scope of the claimed invention, the specification should provide one of skilled in the

art with sufficient information to allow the determination of those structures required or some teaching as to how to obtain those structures without undue experimentation.

The Examiner agrees that a patent need not teach what is well known in the art and acknowledges those enzymes and their corresponding DNAs, which were known at the time of the invention. The Examiner also acknowledges the teachings of the specification and the state of the prior art regarding transformed microorganism using said recombinant genes. However, the Examiner disagrees with the appellants contention that the disclosure provided is sufficient to enable one of skill in the art to practice the full scope of the claimed invention. Regarding appellants arguments that all the genes required to make the recombinant organism are known, but one of ordinary skilled in the art cannot know, how to make the claimed invention without knowing the specific structural feature of the claimed genus of genes encoding any CoA-dependent aldehyde dehydrogenase or any PHA synthase, which would require undue experimentation. Although, the appellants argue that there are ample evidence in the specification regarding claimed genus, however, the art is insufficient to enable the vast scope of appellants claims i.e. appellants are claiming a microorganism comprising any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase gene from any source having any structure, which encompasses many genes including mutants and variants.

The Examiner acknowledges that a considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. However, in the instant case, the amount of information provided is such that it would require undue experimentation to practice the full scope of the claimed invention. While the Examiner agrees that the specification (1)

provides specific genes, (2) recombinant microorganism, (3) method of producing PHA, and (4) working examples, there is no teaching in the specification regarding how to obtain the structures of all the DNAs required or a comprehensive structure/function correlation which would allow one of skill in the art to envision the structure of any DNA encoding any CoA-dependent aldehyde dehydrogenase or any PHA synthase. It is reiterated here that the claim microorganism encompasses DNAs which are unknown in the art. While searching a database would provide those enzymes known in the art, isolating the required DNAs based on the structure of those known in the art (i.e., structureal homology) would be highly unpredictable in view of the unpredictability of the art regarding predicting function baseed solely on structural homology and how small structural modification can significantly affect function. Besides, appellant have not provided any sequence homology data that could provide some common motifs or domains to predict structural features. In addition, a single mutation can change protein function, such as, Branden et al. (1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (1999) and Seffernick et al. (2001), where it is shown that even small amino acid changes result in enzymatic activity changes.

Furthermore, while the argument can be made that the DNAs required for making recombinant microorganism known in the art, it is noted that the amount of information provided

is such that one of skill in the art would have to test an infinite number of DNAs encoding proteins to determine which ones have the desired activity. It is not routine in the art to test an infinite number of proteins which ones have the desired activity. Instead, one of skill in the art would have some knowledge or guidance as to which proteins are more likely to display the desired activity such that amount of screening is limited. Thus, in view of the teachings of the specification, the evidence presented, the unpredictability of the art regarding accurate assigning of function based solely on structural homology and how small structural changes affect function, one cannot reasonably conclude that the claimed invention is enabled by the teachings of the specification.

Claims 18-20

Regarding claims 18, 19 and 20, appellants argues that the organism further comprises recited genes encoding enzymes of acyl-CoA transferase, acyl-CoA synthetase, beta-ketothiolase, and acetoacetyl-CoA reductase in addition to CoA-dependent aldehyde dehydrogenase and PHA synthase, which are well known in the art. Appellants argue that although there is no need for examples, Examples 3-7 describes the production of PHA hydroxyvalerate, wherein the organism expresses the genes recited in claim 18. This is not found persuasive because claims still read on using any acyl-CoA transferase, acyl-CoA synthetase, beta-ketothiolase, and acetoacetyl-CoA reductase having any structure and the claimed invention requires the structures of the genes recited, even though all the genes are well known in the art. In the absence of these genes, one of skill in the art would not know how to make claimed invention commensurate to the scope of the claims. While, it may possible to try to practice the claimed invention from the disclosure of examples 3-7 but it would require undue

experimentation to try infinite possibilities, however, it is impossible to know how to make full scope of the claims.

Claim 21

Regarding claim 21, the Appellants argue that the limitation of the claim to E. coli eutE as the CoA-dependent aldehyde dehydrogenase limits the claim to that which the Examiner has indicated is discussed. However, the rejection has been maintained for this claim because of the lack of structural feature of the heterologous PHA synthase gene recited. Although, claim 21 partially fullfils the enablement requirement in the context of the CoA-dependent aldehyde dehydrogenase, it fails to sufficiently enable the PHA synthase gene recited.

Claims 22 and 23

Regarding claims 22-23, the appellants argue that claims specify recombinant organisms are bacteria or plant, which are suitable for production of PHAs that is well known in the art and although, there is no need for example, Examples 3-7 of the specification describes the production of PHA containing hydroxyvalerate in E. coli. Thus, it would be easy one of ordinary skill in the art, using the knowledge in the art and Appellants discovery of combination of genes necessary to avoid accumulation of propionic acid in the cytosol, to make the claimed organism. in described in the specification. However, the rejection has been maintained because claims are not further limiting the genus of genes encoding any CoA-dependent aldehyde dehydrogenase and any PHA synthase used to make the organism recited in claim 16. Furthermore, MPEP (1205) states that "merely pointing out what a claim recites will not be considered an argument for separate patentibility of the claim". Thius, all arguments above for claims 16 and 17 apply equally to claims 22 and 23.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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